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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/587,899	04/27/2007	Jean-Charles Schwartz	P08977US00/BAS	8912

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STITES & HARBISON PLLC
1199 NORTH FAIRFAX STREET
SUITE 900
ALEXANDRIA, VA 22314

EXAMINER	
SPIVACK, PHYLLIS G	

ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
01/28/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

iplaw@stites.com

Office Action Summary	Application No.	Applicant(s)	
	10/587,899	SCHWARTZ ET AL.	
	Examiner	Art Unit	
	Phyllis G. Spivack	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 November 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 5-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 5-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicants' Response filed November 16, 2010 is acknowledged. New claim 25 is presented. Accordingly, claims 1 and 5-25 are presently under consideration.

Those objections and rejections that are not herein reiterated are withdrawn. The following objection and rejections constitute the only objection and rejections presently applied to the instant claims.

Claims 5-19 and 24 were objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim, in the last Office Action. It was asserted independent claim 1 recites a combination "consisting essentially of" and thus the scope of the claims is limited to the specifically recited compounds and other agents that do not materially affect the basic and novel characteristics of the claimed invention.

Following an amendment to claim 5, the objection under 37 CFR 1.75(c) is withdrawn with respect to claims 5-13. However, the objection of record of method claims 14-19 and new claim 25, i.e., a method for the treatment of acute diarrhea associated with emesis comprising administering the combination of claim 1, is maintained. Dependent claims 14-19 and 25, which are dependent from claim 1, recite "comprising" language and are, therefore, fully open to the inclusion of any other active or inactive component.

Claims 5-19 and 24 were rejected in the last Office under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention Action.

Presently, dependent claims 14-19 and 25 lack clarity in that each employs an open language format that permits the addition of any number of active or inactive agents in the claimed "combination" of independent claim 1. Claim 1 is limited to the combination consisting essentially of racecadotril or dexecadotril with endansetron or granisetron. Therefore, no other agent that materially affects the basic and novel characteristics of the claimed invention is permitted in any of the claims.

Claims 14-19 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

In the last Office Action claims 1 and 5-24 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

It was asserted clear support for the amendment to claim 1, i.e., language drawn to a combination "consisting essentially of" is not provided by Applicants and appears to be absent. See *In re Rasmussen*, 21 USPQ 323 (CCPA 1981).

Applicants argue the specification never needs to include *ipsis verbis*, i.e., word for word, support for claim language and urge that the specification sets forth parameters such that one skilled in the art would understand the accepted transactional phrase "consisting essentially of."

Applicants' argument is not found persuasive. The rejection of record of claims 1 and 5-24, and presently extended to include new claim 25, under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is maintained.

The disclosure as filed fails to set forth what the novel and unobvious character of the instant invention clearly is in order to define what is excluded in view of the "consisting essentially of" wording. A review of the specification on pages 13-14, merely describes an Example in which rats received ondansetron (0.1 mg/kg, p.o.) and racecadotril (40 mg/kg, p.o.) administered together. This combination elicited a nearly complete antidiarrheal effect for 6 - 7 h.

Further, as comparative examples, ondansetron and racecadotril were also administered alone at the same dosages. Ondansetron (0.1 mg/kg, p.o.) was found inactive on this model when administered alone. Racecadotril (40 mg/kg, p.o.) administered alone induced a partial protection for 4 h on this model. Ondansetron at 1 mg/kg was also found inactive on this model but, when associated with 0.1 mg/kg dexecadotril, completely prevented diarrhea.

This Example fails to define what is excluded in view of the "consisting essentially of" wording.

Claims 1 and 5-24 were rejected under 35 U.S.C. 103(a) as being unpatentable over Cojocaru et al., Archives Pediatrics, in view of Cubeddu et al., Alimentary Pharmacol. Ther., and Boige et al., Bulletin du Cancer, in the last Office Action. It was asserted Cojocaru teaches the administration of racecadotril in the treatment of

diarrhea. Racecadotril is an inhibitor of enkephalins (endogenous opioid peptides) that causes a reduction in intestinal secretion. See the Summary, pages 774-775. As an optical isomer of racecadotril, it would have been reasonable to expect dexecadotril to exhibit similar pharmacologic properties. Cubeddu teaches the administration of the 5-HT3 receptor antagonist ondansetron, as an antiemetic in the treatment of gastroenteritis. Boige teaches the administration of ondansetron, granisetron and racecadotril to treat nausea, vomiting and diarrhea. See the discussions under Prevention et traitement specifiques and Diarrhee. Nausea, vomiting and diarrhea frequently occur following the administration of various cancer chemotherapeutic agents and regimens. Boige teaches an oral dosage of granisetron to be 1 mg every 12 hours, an oral dosage of ondansetron to be 8 mg every 8 hours and an intravenous dosage of ondansetron to be 32 mg. Additionally, dosages based on mg/kg body weight are provided. The specific enkephalinase inhibitor acetorphan, which is racecadotril, at a dosage of 300 mg/day, is specifically indicated in late-onset diarrhea.

Applicants argue: Cojocaru does not mention or suggest the combination of racecadotril with an antiemetic; Cubeddu discloses the antiemetic activity of ondansetron but is silent about a combination of ondansetron with racecadotril; and Boige suggests how to achieve an antidiarrheic activity and an antiemetic activity but does not teach or suggest administration of racecadotril with ondansetron for achieving the inhibition of side effects of racecadotril.

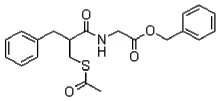
Applicants' arguments are not persuasive. The rejection of record of claims 1 and 5-24 - and presently extended to include new claim 25 - under 35 U.S.C. 103(a),

as being unpatentable over Cojocaru et al., Archives Pediatrics, in view of Cubeddu et al., Alimentary Pharmacol. Ther., and Boige et al., Bulletin du Cancer, is maintained.

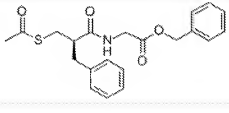
According to Cojocaru, racecadotril is an effective anti-diarrheal agent. Dexecadotril is an optical isomer of racecadotril, which would reasonably be expected to exhibit the same pharmacological properties as racecadotril.

Name	Racecadotril
Synonyms	N-[2-[(Acetylthio)methyl]-1-oxo-3-phenylpropyl]-glycine phenylmethyl ester; Acetorphan; Tiorfan

Molecular Structure



Product Name:	Dexecadotril
Synonyms:	Dexecadotril;N-[(R)-2-[(Acetylthio)methyl]-1-oxo-3-phenylpropyl]glycine benzyl ester;N-[(R)-2-Benzyl-3-(acetylthio)propionyl]glycine benzyl ester;R- Acetorphan;Retorphan
CAS:	**112573-72-5**
MF:	C21H23NO4S
MW.	385.482
EINECS:	
Product Categories:	
Mol File:	112573-72-5.mol



According to Boige, nausea, vomiting and diarrhea may be treated simultaneously following the administration of ondansetron, granisetron and racecadotril.

The prior art recognized the antiemetic and anti-diarrheal properties of the claimed compounds, and *In re Diamond and Kellman*, 149 USPQ 562 (CCPA 1966), supports the obviousness of combining drugs known to be useful for the same purpose. It is standard practice in the pharmaceutical arts to combine ingredients to achieve the same therapeutic endpoint that is established in the prior art for the individual agents.

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this Final Action is set to expire THREE MONTHS from the mailing date of this Action. In the event a first reply is filed within TWO MONTHS of the mailing date of this Final Action and the Advisory Action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the Advisory Action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the Advisory Action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this Final Action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Phyllis G. Spivack whose telephone number is 571-272-0585. The Examiner can normally be reached from 10:30 to 7 PM.

If attempts to reach the Examiner by telephone are unsuccessful after one business day, the Examiner's supervisor, Ardin Marschel, can be reached 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

January 24, 2010

/Phyllis G. Spivack/
Primary Examiner, Art Unit 1614